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July 30, 2008

To: Administrator  
U.S. Environmental Protection Agency  
P.O. Box 1473  
Merrifield, VA 22116  
Attention: Chemical Right-to-Know Program

From: Henry J. Trochimowicz, ScD, DABT  
Delaware Toxicology Associates, Inc.  
10 Briarcreek Court  
Newark, DE 19711

Subject: Cyclohexanone Oxime (CAS No.100-64-1):  
**2<sup>nd</sup> Version** of a Robust Summary/Test Plan for the  
HPV Challenge Program, AR-201

On behalf of DSM Chemicals North America, Inc., I am submitting a revised version of a Robust Summary and a Test Plan for Cyclohexanone Oxime. The preceding documents are attached as WORD XP files and are dated July 29, 2008.

The original versions of the preceding documents were submitted to EPA on March 10, 2006. EPA (Dr. Mark W. Townsend, HPV Chemicals Branch) responded with detailed comments on November 8, 2007. In response to EPA's comments, the attached HPV Robust Summary and Test Plan for Cyclohexanone Oxime have been revised and some details follow.

Based on our original submission, EPA has accepted our claim for a Closed-System Intermediate (CSI) Status for cyclohexanone oxime. As a result, specific testing for the reproductive toxicity endpoint will be waived, but developmental toxicity testing must still be addressed. In addition, based on reassessment of available data and EPA's comments, additional testing in other areas will have to be conducted to satisfy SIDS/HPV endpoints. Therefore, our REVISED TEST PLAN now includes the following studies:

- Oral Developmental Toxicity Screening Study in Rats (OECD TG 421)
- Environmental Fate Testing
  - Stability in Water (Hydrolysis) (OECD TG 111)
  - Ready Biodegradation (OECD TG 301)
  - Fugacity Calculations (based on current p/c data)
- Ecological Studies
  - 96-Hr LC50 in Fish (OECD TG 203)
  - 48-Hr EC50 in *Daphnia magna* (OECD TG 202)
  - Algae Growth Inhibition (OECD TG 201)

Relative to our REVISED ROBUST SUMMARY, additional information has been added in accordance with EPA Comments. Under Acute Toxicity, a recently-obtained, well-conducted oral toxicity study in rats has been added as the "Preferred Result" and some additional information detail is now included under "Supporting Data". In regard to "Genotoxicity", the detailed data presented on gene mutation and chromosome aberration are adequate to satisfy this endpoint. The additional supporting studies (without detail) support our conclusion, based on a weight-of-evidence approach, that cyclohexanone oxime is not a mutagen. Finally, as EPA reviewers suggested, we added additional information on histopathological examination of reproductive organs to the Repeated-Dose Toxicity section; the same data was also summarized in less detail in the section on Reproductive Toxicity. In conclusion, with the exception of developmental toxicity (study to be conducted), the data now available in our revised Robust Summary adequately satisfies the remaining "Mammalian Toxicity" endpoints.

Since several experimental studies are proposed in the REVISED TEST PLAN, your prompt response to this submission would be greatly appreciated. Please address any questions or comments concerning this submission to:

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